Significant Publications


Rac GTPases have been implicated in the regulation of diverse functions in various blood cell lineages, but their role in T-cell development is not well understood. We have carried out conditional gene targeting to achieve hematopoietic stem cell (HSC)– or T-cell lineage–specific deletion of Rac1 or Rac1/Rac2 by crossbreeding the Mx-Cre or Lck-Cre transgenic mice with Rac1loxp/lox or Rac1loxp/lox;Rac2−/− mice. We found that (1) HSC deletion of both Rac1 and Rac2 inhibited production of common lymphoid progenitors (CLPs) in bone marrow and suppressed T-cell development in thymus and peripheral organs, whereas deletion of Rac1 moderately affected CLP production and T-cell development. (2) T cell–specific deletion of Rac1 did not affect T-cell development, whereas deletion of both Rac1 and Rac2 reduced immature CD4+CD8+ and mature CD4+ populations in thymus as well as CD4+ and CD8+ populations in spleen. (3) The developmental defects of Rac1/Rac2 knockout T cells were associated with proliferation, survival, adhesion, and migration defects. (4) Rac1/Rac2 deletion suppressed T-cell receptor–mediated proliferation, IL-2 production, and Akt activation in thymocytes. Thus, Rac1 and Rac2 have unique roles in CLP production and share a redundant but essential role in later stages of T-cell development by regulating survival and proliferation signals.


Individuals with sickle cell disease (SCD) have increased inflammation, a high incidence of airway hyperreactivity...
(AH), and increased circulating leukotrienes (LT). We show that expression of 5-lipoxygenase and 5-lipoxygenase activating protein (FLAP), key catalytic molecules in the LT pathway, were significantly increased in peripheral blood mononuclear cells (MNCs) in patients with SCD, compared with healthy controls. Placenta growth factor (PIGF), elaborated from erythropoietin cells, activated MNC and THP-1 monocytic cells to induce LT production. PIGF-mediated increased FLAP mRNA expression occurred via activation of phosphoinositide-3 (PI-3) kinase, nicotinamide adenine dinucleotide phosphate (NADPH) oxidase, and hypoxia inducible factor-1 (HIF-1). HIF-1 small interfering RNA (siRNA) reduced PIGF-induced FLAP expression. FLAP promoter-driven luciferase constructs demonstrated that PIGF-mediated luciferase induction was abrogated upon mutation of HIF-1 response element (HRE), but not the nuclear factor- B (NF- B) site in the FLAP promoter; a finding confirmed by chromatin immunoprecipitation (ChIP) analysis. PIGF also increased HIF-1 binding to the HRE in the FLAP promoter. Therefore, it is likely that the intrinsically elevated levels of PIGF in SCD subjects contribute to increased LT, which in turn, mediate both inflammation and AH. Herein, we identify a mechanism of increased LT in SCD and show HIF-1 as a hypoxia-independent target of PIGF. These studies provide new avenues to ameliorate these complications.


Nucleoslopin (NPM) is frequently overexpressed in leukemias and other tumors. NPM has been reported to suppress oncogene-induced senescence and apoptosis and may represent a therapeutic target for cancer. We fused a NPM-derived peptide to the HIV-TAT (TAT-NPM C) and found that the fusion peptide inhibited proliferation and induced apoptotic death of primary fibroblasts and preleukemic stem cells. TAT-NPM C down-regulated several NF- B–controlled survival and inflammatory proteins and suppressed NF- B–driven reporter gene activities. Using an inflammation-associated leukemia model, we demonstrate that TAT-NPM C induced proliferative suppression and apoptosis of preleukemic stem cells and significantly delayed leukemic development in mice. Mechanistically, TAT-NPM C associated with wild-type NPM proteins and formed complexes with endogenous NPM and p65 at promoters of several antiapoptotic and inflammatory genes and abrogated their transactivation by NF- B in leu-kemic cells. Thus, TAT-delivered NPM peptide may provide a novel therapy for inflammation-associated tumors that require NF- B signaling for survival.
We have revealed an essential role of Rac1/Rac2 GTPases in T-cell development by regulating unique cell cycle and survival pathways (Guo et al., Blood 2008).

Paul Andreassen, PhD
The Andreassen lab has shown that monoubiquitinated FANCD2 is required for homologous recombination at telomeres in a subset of cancer cells (Fan et al. 2009 Nucleic Acids Res.)

Christopher Baum, MD
In a prospective study involving ~ 100 patients with acute leukemia, the Baum lab has identified neurotrophin receptor expression as a novel prognostic marker (Li et al., Blood 2009).

In a murine model, the Baum lab demonstrated that cell-intrinsic factors play a major role in the risk of insertional leukemia induction by gene vectors (Kustikova et al., Mol Ther 2009).

Together with two colleagues (Dr. Ute Modlich and Sabine Knoess), Baum lab has obtained a prestigious award of the German Research Foundation (DFG) for research to replace, reduce and refine animal experiments (50000 € Ursula M. Haendel animal protection award 2009.

Jose Cancelas, MD, PhD
Demonstration that mastocytosis in a murine model of chronic eosinophilic leukemia/mastocytosis induced by expression of the fusion gene FIP1L1/PDGFRa depends on SCF/c-kit signaling and subsequent synergistic activation of Akt. This manuscript is a result of a very successful collaboration with the Division of Allergy/Immunology of CCHMC (Dr. M. Rothenberg). (Yamada et al,Blood. 2008).

Marie-Dominique Filippi, PhD
We have identified and characterized a critical signaling module regulating blood neutrophil migration - the mechanisms and essential features of neutrophil polarity regulation by Cdc42.

Hartmut Geiger, PhD
Demonstration of phenotypes of aged hematopoietic stem cells in vivo, particularly the “hyperactivity” in terms of moving on the bone marrow niche (Blood 2009).

Elke Grassman, PhD
We have provided certification testing for a clinical vector and completed mouse safety studies to support and IND for use in a multi-institutional gene transfer trial for the treatment of severe combined Immunodeficiency (X-SCID). Data from the mouse safety studies was presented at the ASGT’s 12th annual meeting, May27-30, 2008 in San Diego, CA in an oral abstract session.

We have developed high complexity assays to support production development of lentiviral vector products.

We have initiated mouse safety studies for a gene transfer trial for sickle cell anemia.

Fukun Guo, PhD
Discovered a unique role of the Rho GTPase Cdc42 in regulating B-cell development and activation, specifically in modulating pre-pro-B cell survival and cell cycle progression in the bone marrow and spleen (Guo F, et al. Blood, 2009, in press).

Punam Malik, MD
We identified the mechanism of reduction in titers from lentivirus vectors carrying chromatin insulator elements in the 3' LTR. (Molecular Therapy 2009).

We generated a novel human gamma-globin gene vector for genetic correction of sickle cell anemia in a humanized sickle mouse model and identified critical determinants for successful correction. (Blood 2009).

We assessed the genotoxic potential of gene therapy vectors for hemoglobinopathies (Molecular Therapy 2009).

We showed that placenta growth factor augments endothelin-1 and endothelin-B receptor expression via hypoxia-inducible factor, linking erythropoiesis, pulmonary hypertension and inflammation in sickle cell disease. (Blood 2008).

We also showed that placenta growth factor induces 5-lipoxygenase-activating protein expression via hypoxia-inducible factor-1α to increase leukotriene formation in sickle cell disease. (Blood 2009).

Ruhikanta Meetei, PhD
Discovery of a new component of BTB complex called BLAP18/RMI2 and implication of its role in a cancer-predisposing condition called Bloom’s Syndrome (Gene & Dev 2008).

Discovery that one FA patient (EUFA867) with biallelic mutations in FANCM also carries biallelic mutations in FANCA.
Dao Pan, PhD

Lysosomal enzyme in red project: We are the first to demonstrate that erythroid cells, transduced with a tissue-specific lentiviral vector, can produce and release a lysosomal enzyme efficiently and continuously at supra-physiological levels in the circulation, and can also achieve phenotypic correction in peripheral organs and the CNS of mouse model with Hurler syndrome (manuscript submitted).

KCC profiling project—in collaboration with Dr. Joiner: the changes of expression from three KCl cotransporter genes and with different splicing isoforms were studied during human and murine erythroid differentiation, suggesting the KCC3a is dominant in human red blood cells (manuscript in preparation).

Qishen Pang, PhD

Role of FANCA in HSC/P cell migration and homing – We recently demonstrated a cell-autonomous defect of HSC/P cells from FA-A patients in homing and identified a failure of the hematopoietic supportive capacity of FA-A stromal cells. A manuscript based on this work was published in Blood.

Functional interaction between FA and p53 pathways in oxidative and oncogenic stress responses – We studied the function of FA proteins in oxidative DNA damage and oncogenic stress response and found that BM cells from Fanca-/- and Fancc-/- mice elicited a p53-dependent growth arrest and DNA damage response to oxidative and oncogenic stress. We published these results in Cancer Res.

Identification of NFκB activator during FA leukemogenesis – We showed B-controlled survival and that a NPM antagonist down-regulated several NF-κB-driven reporter gene activities. Akinflammatory proteins and suppressed NF-κB manuscript based on this work was published in Blood

Nancy Ratner, PhD

A discovery that expansion of an EGFR-expressing early glial progenitor contributes to neurofibroma formation. It provides new insights to therapeutic strategies targeting this tumor initiating cell population (Cell Stem Cell 2009)

Jianqiang Wu, PhD

Role of EGFR in neurofibroma development in Neurofibromatosis type 1 (Williams, Wu et al, Cell Stem Cell. 2008, 3(6):658-69.)

Preclinical therapeutic trials of RAD001 and BEZ-235 on a neurofibroma mouse model

Division Collaboration

Collaboration with Developmental Biology
Collaborating Faculty: C.-Y. Kuan; K. Campbell

Collaboration with Hematology/Oncology
Collaborating Faculty: Frank Smith

Collaboration with Immunobiology
Collaborating Faculty: D. Hildeman
Rac1 and Rac2, play redundant and critical role in T-cell development. Blood 112(5):1767-75.

Collaboration with UC Cancer Cell Biology
Collaborating Faculty: Erik Knudsen

Collaboration with Allergy/Immunology
Collaborating Faculty:
Analysis of the signaling mechanisms responsible for FIP1L/PDGFRa-induced chronic eosinophilic leukemia and mastocytosis.

Collaboration with Pulmonary
Collaborating Faculty: Tim LeCras
Tim Le Cras supports the Geiger lab in better understanding the role of EGFR signaling in hematopoiesis.

Collaboration with UC
Collaborating Faculty: Peter Stambrook
We work together with the Stambrook lab to understand DNA repair pathways in hematopoietic stem cells.

Collaboration with UC
Collaborating Faculty: Anil Mennon
In experiments with the Menon lab we determine the influence of the mother on the epigenetic make-up of hematopoietic stem cell during development.

Collaboration with Hematology/Oncology; Boston Children's Hospital; Institute of Child Health in London; Necker Hospital
Collaborating Faculty: Lisa Filipovich; David Williams; Adrian Thrasher; Alan Fisher
which will be sites conducting the Phase I X-SCID gene transfer trial and using the clinical vector produced at CCHMC, translational cores.

Collaboration with Immunobiology
Collaborating Faculty: David Hildeman; Lee Grimes
They have performed some assays.

Collaboration with Hematology/Oncology
Collaborating Faculty: Clint Joiner; Karen Kalinyak; Eric Mullins; Susanne Wells
Sickle Cell Research

Collaboration with Developmental Biology
Collaborating Faculty: Jay Degen; James Wells
Sickle Cell Research

Collaboration with Immunobiology
Collaborating Faculty: Marsha Wills-Karp
Sickle Cell Research

Collaboration with Pulmonary Medicine
Collaborating Faculty: William Hardie; Gary McPhail; Carolyn Kercsmar
Sickle Cell Research

Collaboration with Cardiology
Collaborating Faculty: Bill Gottliebson; Janaka Wansapura; Woody Benson; Jeffrey Towbin
Sickle Cell Research

Collaboration with Genetics
Collaborating Faculty: William Nichols
Sickle Cell Research

Collaboration with UC
Collaborating Faculty: Robet Franco; George Atweh; Rupak Bannerjee
Role of Placenta growth factor in sickle acute chest syndrome

Collaboration with Immunobiology
Collaborating Faculty: Lee Grimes
Mouse modeling of human T-ALL

Collaboration with Molecular Immunology
Collaborating Faculty: Claire Chougnet; Julio Aliberti
Characterization of a new xenograft model that greatly potentiates human T-cell development from human CD34+ cells. May prove useful for HIV research, graft vs host disease, analysis of in vivo human T-cell development and modeling human T-cell leukemia.

Collaboration with Human Genetics
Collaborating Faculty: Xiaoyang Qi
Lead compound testing of a patented, proprietary anti-cancer compound in human leukemia xenograft models.

Collaboration with Developmental Biology
Collaborating Faculty: Jim Wells
Mechanistic dissection of the activation of B-catenin in AML1-ETO-expressing cells

Collaboration with Hematology/Oncology
Collaborating Faculty: Clinton Jointer

Mechanistic dissection of the activation of B-catenin in AML1-ETO-expressing cells
to study the expression of ion transporter (KCC) during erythropoiesis and potential therapeutic effect by
manipulation of KCC using shRNA approach on Sickle Cell Diseases.

Collaboration with UC
Collaborating Faculty: Robert Franco
to study the expression of ion transporter (KCC) during erythropoiesis and potential therapeutic effect by manipulation of KCC using shRNA approach on Sickle Cell Diseases.

Collaboration with Hematology/Oncology
Collaborating Faculty: Theodosia Kalfa
to provide expertise on real-time RT-qPCR in her project studying RAC expression during erythropoiesis, and to use her expertise in our project studying red cell-specific expression of lysosomal enzyme.

Collaboration with Developmental Biology
Collaborating Faculty: Alex Kuan
to provide expertise/work on lentiviral vector construction and LV-mediated gene transfer into isolated neuronal cells for his project; and on large-molecule delivery across brain-blood-barrier (BBB) using his expertise in brain pathology.

Collaboration with UC
Collaborating Faculty: David Hui
for his expertise on LDL receptor superfamily and apoE metabolism to study large-molecule delivery across BBB.

Collaboration with UC
Collaborating Faculty: Keith Crutcher
who provide his expertise on neuroanatomy and toxicity in our project on large-molecule delivery across BBB.

Collaboration with Ohio State University
Collaborating Faculty: Greg Lesinski; William Carson
to provide expertise/work on shRNA lentiviral vector construction and LV-mediated gene transfer into primary cells in their project studying the function and regulation of STAT5 in immune system.

Collaboration with Human Genetics
Collaborating Faculty: Ying Sun; Greg Grabowski
to collaborate on CNS abnormality in murine MPS models.

Collaboration with Biomedical Informatics
Collaborating Faculty: Bruce Aronow

Collaboration with Hematology/Oncology
Collaborating Faculty: John Perentesis; Tim Cripe

Collaboration with UC/GRI
Collaborating Faculty: George Thomas; Sara Kozma; William Seibel

Collaboration with Developmental Biology
Collaborating Faculty: Brian Gebelein
MPNST Gene Project

Collaboration with Radiology
Collaborating Faculty: Diana Lindquist; Scott Dunn
Magnetic resonance image (MRI) monitors neurofibroma development in a neurofibroma mouse model.

Collaboration with Molecular Immunology
Collaborating Faculty: Chris Karp
Modification of cystic fibrosis lung disease severity by polymorphisms in genes regulating neutrophil function. Nature 2009
Collaboration with Blood Bone Marrow Transplantation

Collaborating Faculty: A. Filipovich


Faculty Members

Yi Zheng, PhD, Professor; Division Director; Endowed Chair; Program Leader
Research Interests: Signaling Program

Paul Andreassen, PhD, Assistant Professor
Research Interests: Leukemia Biology

Mohammed Azam, PhD, Research Assistant Professor
Research Interests: Cancer Pathology

Jose Cancelas, MD, PhD, Associate Professor; Program Leader
Research Interests: Stem Cell Program

Marie-Dominique Filippi, PhD, Research Assistant Professor
Research Interests: Stem Cell Program

Hartmut Geiger, PhD, Research Associate Professor
Research Interests: Stem Cell Program

Elke Grassman, PhD, Assistant Professor; Director, TTDSL
Research Interests: Signaling Program

Gang Huang, PhD, Research Assistant Professor
Research Interests: Cancer Pathology

Punam Malik, MD, Associate Professor; Program Leader; Director of Cores
Research Interests: Molecular and Gene Therapy Program

Ruhikanta Meetei, PhD, Assistant Professor
Research Interests: Signaling Program

James Mulloy, PhD, Research Associate Professor
Research Interests: Leukemia Biology Program

Dao Pan, PhD, Research Assistant Professor
Research Interests: Molecular and Gene Therapy Program

Qishen Pang, PhD, Associate Professor
Research Interests: Signaling Program

Nancy Ratner, PhD, Professor; Program Leader; Endowed Chair
Research Interests: Cancer Biology Program

Lilith Reeves, MS, Field Service Associate Professor; Director
Research Interests: Translational Cores

Tilat Aziz Rizvi, PhD, Research Assistant Professor
Research Interests: Cancer Biology Program

Johannes van der Loo, PhD, Field Service Assistant Professor
Research Interests: Vector Production

Jianqiang Wu, MD, Research Instructor; Cancer Biology

Joint Appointment Faculty Members

Christopher Baum, MD, Adjunct Associate Professor
Hanover Medical School
Gene Therapy

Tim Cripe, MD, PhD, Associate Professor
Hematology/Oncology
Musculoskeletal Tumor, Translational Research Trials

Timothy Crombleholme, MD, Professor
Surgery
Molecular Fetal Therapy

Stella Davies, MB, BS, PhD, MRCP, Professor
Hematology/Oncology
Blood and Marrow Transplantation, Leukemia Biology

Rachid Drissi, PhD, Research Assistant Professor
Hematology/Oncology
Oncology

Leighton Grimes, PhD,  Research Associate Professor
Immunobiology
Cancer Pathology

Clinton Joiner, MD, PhD,  Professor
Hematology/Oncology
Sickle Cell

Theodosia Kalfa, MD, PhD,  Assistant Professor
Hematology/Oncology
Red Blood Cells and Sickle Cells

Joe Palumbo, MD, Research Associate Professor
Hematology/Oncology
Hematology

Janos Sumegi, MD, PhD,  Professor
Hematology/Oncology
Immune Deficiency and Histiocytosis

Susanne Wells, PhD, Assistant Professor
Hematology/Oncology
Cancer Biology

David Williams, MD, Adjunct Professor
Children's Hospital Boston
Stem Cell Biology

Trainees

- Zsuzsanna Adam, PhD, 2006, University of Debrecen, Hungary
- Shirin Akhter, PhD, 2003, University of Windsor, Windsor Canada
- Abdulla Mahmood Ali, PhD, 2004, Indian Institute of Science, India
- Paritha Arumugan, PhD, University of Madras, Chennai, TamilNadu, India
- Suchitra Basu, PhD, 2008, University of Toledo
- Emily Bosco, PhD, 2006, University of Cincinnati
- Fu-Sheng Chou, MD, 2004, OSU
- Eric Dickerson, 
- Changhu Du, MD, PhD, 2004, Guangzhou Institute of Respiratory Disease, Gangzhou Medical School, China
- Wei Du, MD, PhD, 2007, Graduate School of Medicine, Tohoku University, Japan
- Marthe-Sandrine Eiymo Mwa Mpollo, Msc, University of Toronto
- Satyam Eleswarapu, PhD, MS, DVM, 2009, Blacksburg
- Qiang Fan, PhD, 2002, SUNY at Stony Brook
- Yuxin Feng, PhD, 2007, BioChain Institute
- Gabriel Ghiaur, 
- Brittany Goetz, 
- Daniel Gonzalez-Nieto, PhD, 2003, Hospital Ramon & Cajal, Madrid, Spain
- Matthew Grogg, PhD, 2006, University of Dayton
- Li Guo, PhD, 2007, Institute of Neuroscience, Chinese Academy of Sciences, Shanghai, China
- Marnie Hall, PhD, 2005, University of Cincinnati, College of Medicine
- Tomoyasu Higashimoto, PhD, 2006, University of Southern California
- Adrienne Hontz, PhD, 2008, The University of Kansas Medical Center
- Walter Jessen, PhD, 2004, 
- Gunnar Johanson, MS, 2002, Umea Universitet, Sweden
- Edwin Jousma, Msc, 2003, University of Amsterdam, the Netherlands
- Nathan Kolasinki, 
- Jie Li, PhD, Academy of Sciences, China
- Kevin Link, PhD, 2007, University of Cincinnati
- Anuj Mankad, PhD, 2006, Oregon Health and Science University, Portland, Oregon
- Filippo Marchioni, PhD, 2005, University of Bologna
- Debra Mayes, PhD, 2006, University of Arkansas for Medical Sciences
- Jaime Melendez, PhD, 2001, University of Chile
- Kyle Mitts, BS, 2009, Xavier University
Richard Morreale, PhD, 2007, University of California
Whitney Nordheim, ,
Deanna Patmore, BS, 2007, Voorhees College
Melissa Rawe, , University of Cincinnati
Amitava Sengupta, PhD, 2008, Jadavpur University/Saha Institute of Nuclear Physics Kolkata, India
Xun Shang, PhD, 2004, National University of Singapore
Thiyam Singh, PhD, 2003, University of Maryland at Baltimore
Nisha Sipes, MS, 2004, University of Cincinnati
Nambirajan Sundaram, PhD, 2008,
Fabrizia Urbinati, PhD, 2005, University of Modena, Italy
Shiv Viswanathan, PhD, 2003, University of Cincinnati
Daren Wang, PhD, 2004, Akita University Medical School, University of China Medical School, China
Junping Wei, MD, 2004, Heibei Medical University School of Medicine,
Jon Williams, BS, 2001, Muskingum College
Yang Mingyan, ,
Zhao Xinghui, ,

**Significant Accomplishments**

**Overview**

Division of Experimental Hematology and Cancer Biology continues the tradition to publish high quality papers and to win grant supports in 2008-2009. The following projects, encompassing multiple programs and disciplines in the division, represent some of the highlights.

**Neurofibromatosis**

Neurofibromatosis is a common autosomal dominant inherited disease symptomized by nerve tumors called neurofibromas, whose cellular origin had not been known. A team of researchers led by Dr. Nancy Ratner reported in *Cell Stem Cell* that Nf1 gene mutation expands a peripheral nerve progenitor, which confers neurofibroma tumorigenic potential. They characterized the normal mouse peripheral nervous system embryonic dorsal root ganglion progenitor populations, and found that they require signaling from the EGFR tyrosine kinase. Nf1 loss of function amplifies this progenitor pool, which becomes hypersensitive to growth factors and confers tumorigenesis. Mouse neurofibromas, but not normal nerve, contain a progenitor population with similar growth requirements, potential, and marker expression. Following the mouse model studies, the team identified cells in human neurofibromas cells with progenitor properties. This study suggests that expansion of an EGFR-expressing early glial progenitor contributes to neurofibroma formation, and provides new insights to therapeutic strategies targeting this tumor initiating cell population.

**Bloom's Syndrome**

Mutations in the BLM gene give rise to Bloom’s syndrome, a rare genetic disorder characterized by severe growth retardation, immunodeficiency, anemia, and reduced fertility. Importantly, Bloom’s patients develop various types of cancers often at a young age. BLM encodes a DNA helicase, that associates with Topo IIIα and BLAP75/RMI1 to form a large molecular complex. This complex serves to prevent chromosomal aberrations and rearrangements. Dr. Ruhikanta Meetei and colleagues reported in *Genes & Development* the discovery of a new component of this complex called BLAP18/RMI2. This molecule represents a new protein that is important for DNA complex stabilization and checkpoint response, and is required for the maintenance of a stable genome in cells. The identification of this protein playing a critical role in Bloom’s syndrome illustrates the intricacies of molecular mechanisms that ensure genomic stability and reveals new mechanism how a destabilized genome may be associated with developmental defects such as growth retardation, immunodeficiency, and infertility, as well as cancer.

**Division Publications**

31. Wise-Draper TM, Mintz-Cole RA, Morris TA, Simpson DS, Wikenheiser-Brokamp KA, Currier MA, Cripe TP, Grosveld GC, Wells SI. Overexpression of the cellular DEK protein promotes epithelial transformation in vitro and


Grants, Contracts, and Industry Agreements

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<th>Grant and Contract Awards</th>
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<td><strong>CANCELAS, J</strong></td>
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<td>Inhibition of Rac GTPases in the Therapy of Chronic Myelogenous Leukemia</td>
<td>$144,315 / $450,000</td>
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<td>Rac in p190-BCR/ABL Leukemia</td>
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<td>Rac GTPase Inhibition in Chronic Myelogenous Leukemia</td>
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<td>The Role of the Small GTPase RHOA in Hematopoietic Stem Cell Engraftment</td>
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<td>Genomic Integrity and DNA-Repair Pathways in Aging</td>
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<td>Pathways to Mutagenesis in Vivo and in Stem Cells</td>
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<td>Genetic and Biochemical Evaluation of Rac1 GTPase Signaling Mechanism in Primary Cells</td>
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<td>Core A</td>
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<tr>
<td>Cripe, Timothy</td>
<td>Core B</td>
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<td>Rizvi, Tilat</td>
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**Therapeutic Targets for Peripheral Nerve Tumors**  
Department of Defense - Army  
W81XWH-09-1-0135  
03/01/09 - 02/28/11  
$219,843 / $439,686

**Identification of Drug Targets for NF1**  
National Institutes of Health (Dartmouth College)  
R21 NS 060940  
02/15/09 - 01/31/11  
$10,629 / $21,258

**REEVES, L**  
**FDA-NTP Studies of Insertional Mutagenesis**  
National Institutes of Health (Battelle Memorial Institute)  
HHSN29120055536  
09/05/08 - 08/15/09  
$92,711 / $132,647

**SENGUPTA, A**  
**Rac GTPases and BMI-1 CML Stem Cell Niche**  
Lady Tata Memorial Trust  
10/01/08 - 09/30/09  
$45,717 / $45,717

**WEI, J**  
**A Novel Model of Poor Prognosis Infant Leukemia Using Primary Human Blood Stem Cells**  
American Society of Hematology  
07/01/07 - 12/31/08  
$50,000 / $100,000

**ZHENG, Y**  
**Cell Type and Stimulus-Specific Role of Cdc42 in Blood**  
National Institutes of Health  
R01 HL 085362  
07/01/06 - 05/31/11  
$242,750 / $1,221,000

**Rac of GTPases as Targets in Lymphomagenesis**  
National Institutes of Health  
R01 CA 125658  
02/10/07 - 01/31/12  
$190,000 / $950,000

**Training Program in Pediatric Hematologic and Oncologic Diseases**  
National Institutes of Health  
T32 HL 091805  
09/01/08 - 08/31/13  
$151,392 / $779,736

**Rac GTPase-Specific Small Molecule Inhibitors**  
National Institutes of Health  
R01 CA 141341  
03/24/09 - 01/31/14  
$169,934 / $817,982

**Rac GTPases in the Mammalian Brain Development**  
National Institutes of Health  
R01 NS 056435  
07/01/08 - 06/30/12  
$80,000 / $400,000

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| Current Year Direct Receipts | 0 |

**Service Collaborations**

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<td>GOSH</td>
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<td>Necker</td>
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<td>GeneDx</td>
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<td>Hoxworth (QC, CAP, CFU, CD, QC)</td>
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<td>Domestic and Foreign</td>
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**Total** 6,332,861

**Current Year Direct** 654,943

### Funded Collaborative Efforts

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<th>Description</th>
<th>Awarding Agency</th>
<th>Principal Investigator</th>
<th>Status</th>
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<td>Ratner, N</td>
<td>Cincinnati NF1 Preclinical Testing Center</td>
<td>The Children's Tumor Foundation</td>
<td>Cripe, Timothy</td>
<td>06/01/09 - 05/31/11</td>
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<td>Cancelas, J</td>
<td>Transcriptional Control of Respiratory Epithelial Progenitor Cells</td>
<td>National Institutes of Health</td>
<td>Whitsett, Jeffery</td>
<td>08/28/07 - 06/30/11</td>
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<td>Pan, D</td>
<td>Cincinnati Comprehensive Sickle Cell Center</td>
<td>National Institutes of Health</td>
<td>Joiner, Clinton</td>
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**Total** 6,332,861